FULLERTON (E.B.)

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BY

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The Points of the Argument.

The strong points in the following papers are, in the writer's opinion, as follows:

The test accidently made in 1873 in the case that I prescribed for but did not see; the more extensive test-experiment made by Dr. Schlömann in San Antonio, Texas, in 1866; the fresh vegetable and sauerkraut test in the Tennessee Penitentiary in 1873.

The constant reference by the different authorities to the analogies between, or identity of, cholera and malarial disorders. Why this reiteration unless the success of the remedy in cholera strongly suggested or supported the theory of the other disease?

The pointing out the fallacy of using the remedy hypodermically, and the after ability to show about when and where the departure was made, from the earlier method of administration by the mouth, to the unphilosophical intravenous and hypodermic methods.

The general trend of the treatment in the worst cases to a mortality of about 20 per cent. only, which led me to assert that the method of administration in the Stillé list with its 63 per cent. of mortality must have been the hypodermic, and to ask, as well, for a revised translation of the Putelli article with its at-first-asserted death rate of over 46 per cent.

The facts and figures brought to prove, that the disease treated in the penitentiary at Nashville, Tenn., in 1873, could have been nothing other or less, than malignant Asiatic Cholera, kept in check by the constant administration of quinine in sufficient doses.

The figures showing the impossible doses of other remedies necessary to equal in inhibitory effect forty grains of quinine, and thereby proving this remedy to be the most promising, in what wiser men, similarly circumstanced, have termed "the state of the argument."

The fact that the proofs come, empiric end foremost, making the method of reasoning inductive and not synthetic and seductive merely.

The further fact that it is no new and untried remedy, with hypothetical potentialities, to which attention is here directed, but one which, by reason of its control over one low form of organism, has rendered habitable the great interior valley of The Light Continent, and will be as necessary as gunpowder, in the conquest and civilization of "The Dark."

The articles are, with corrections, chiefly verbal, as they appeared in the New York Medical Record.

E. B. F.

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In the volume entitled "The Cholera Epidemic of 1873 in the United States," under the head of "Notes on Treatment," quinine is referred to as having been given in small doses, at uncertain intervals, by two writers, and by one in conjunction with atropine, amounts not stated.

In Dr. Edward O. Shakespeare's "Report on Cholera in Europe and India" no reference is made to quinine in the chapter in which treatment is considered, but it was used in the cities of Teruel, Toledo, and Tembleque in Spain during 1884. The dose is not mentioned in any case, nor the method, except in one only, where it was the hypodermic, with a strong inference that it was so used in the two other cities. The journals at the time gave the dose as fifteen grains, administered hypodermatically. When we recall two well-known facts —first, that the Koch germ is found inside the intestine and not in the blood, and secondly, that the direction of quinine is toward the kidneys, but little, under ordinary circumstances, escaping with the fæces —a reason for failure when administered hypodermatically is apparent. In 1884 Koch places quinine next to mercuric chloride in development-inhibiting (not disinfectant) power, the former acting in strength of 1 to 5,000, the latter in that of 1 to 100,000. In other words, one-half grain of the mercurial is the required equivalent for growth-inhibition of ten grains of quinine. When it is recollected that the lethal

dose of the one is about two grains, and that of the other about two ounces, the disparity for practical effects is apparent. If five grains of quinine can inhibit the development of the spirillum in three pints of rice-water discharge *in situ*, what ill effect can be apprehended from four or six times that amount? All this, however, is "reasoning after the event" with the writer.

In the epidemic of 1873 the use of quinine was early begun in cases coming under my care in this city. In over thirty cases of choleraic diarrhœa there was only one that proved refractory to the quinine treatment, developing into what under the old nomenclature would be called a mild case of cholera. Of the severer or typical form of the disease I had five cases, in all of which quinine was given in doses of seven and one-half grains in solution in the usual way, by means of a sufficient quantity of aromatic sulphuric acid; and this dose was repeated at intervals of an hour and a half or two hours until the symptoms were under control, then in smaller doses at longer intervals. Ice was allowed from the first in guarded quantities, and, so soon as the tendency to vomit was sufficiently controlled, ice-water.

In some cases a small amount of morphine was given, in others not. In all cases there was decided improvement after the first dose, and a steady abatement of the symptoms as the treatment progressed. The patient in whom the disease was, perhaps, farthest advanced when treatment was commenced vomited but three times and purged but twice after the first dose was given. In this case, with the typical pulse, thirst, cramps in extremities, sunken countenance, and loss of voice, the vomiting was incessant, and the constant discharge from the bowels had penetrated the mattress and stood in a pool on the floor beneath. In one case in which I was consulted by the physician in attendance, quinine was exhibited to the extent of fourteen grains in pill form. The patient's symptoms, typical as described, were controlled for forty-eight hours, he returning to his place of business on the second day. At the end of the above mentioned period the symptoms returned and he died in the course of a few hours, no quinine having been administered during the relapse.

While aware of the danger in forming conclusions too radical on the success of treatment in so limited a number of cases, and also bearing in mind that epidemic diseases differ in tractability and severity during different seasons of their prevalence, and at differing periods of the same epidemic, yet I have been unable to rid my mind of the impression, strongly made nineteen years ago, that the quinine

treatment had much to do with the results above recorded. That the disease prevalent in Columbus, O., in 1873 was of no mild type is shown by the report of Dr. Halderman, where, out of one hundred and thirty-eight cases recorded, there were ninety deaths, a mortality of more than sixty-five per cent.

Permit me strongly to urge upon the physicians now treating the disease in quarantine or hospital that they try the remedy. I would suggest that one drachm be dissolved in three ounces of water by means of a sufficient quantity of dilute or aromatic sulphuric acid, and that of this solution a tablespoonful be administered and at once repeated if vomiting occurs, and afterward at intervals of an hour and a half, until thirty grains have been taken, and thereafter pro re nata. If judged best, a small amount of morphine may be added, or a few drops of chlorodyne—their necessity I doubt. There are a few provisos:

1. The ten grain doses should be in solution, so that in case of vomiting some may be retained.

2. That the patient be not already moribund from toxæmia, or in pulseless collapse.

While the discoveries of the last few years render the theory of Dr. Cunningham, that cholera is "malaria perniciosa," untenable, there is nothing as yet by which we may infer that the treatment may not be essentially the same.

[From the Medical Record, December 10, 1892.]

SECOND PAPER.

A former communication,[1] giving my own experience during the cholera epidemic of 1873, contained a comparison between quinine and mercuric chloride, as to amounts necessary to inhabit the growth of the cholera spirillum. Since then, in a ten minute discussion of the "Treatment of Cholera," before the Medical Section of the Mississippi Valley Medical Association, the following more complete list with comparative amounts was given. The list of inhibitory amounts is from that of Professor Koch, made public in 1884, with the exception of tannic acid, from Cantani, and salol, from Lowenthal, the estimate for the latter being based upon his lowest amount for sterilizing or (as

[1] Medical Record, October 1, 1892.

it did not always sterilize) inhibiting the growth of the germ. One grain of quinine, which inhibits in strength of 1 to 5,000, is used as the standard of comparison, and results are given in round numbers, as inhibitory amounts doubtless were.

INHIBITORY LIST WITH DEDUCTIONS.

Alcohol, 10 to 100	Quinine,	1	grain	= 1 fluid ounce.
Alum, 1 to 100	"	1	"	= 50 grains.
Camphor, 1 to 300	"	1	"	= $16\frac{2}{3}$ grains.
Ac. carbolic, 1 to 400	"	1	"	= $12\frac{1}{2}$ grains.
Oil peppermint, 1 to 2,000	"	1	"	= $2\frac{1}{2}$ *M.*
Sulph. copper, 1 to 2,500	"	1	"	= 2 grains.
Salol, 1 to 100	"	1	"	= 50 grains.
Tannin, 1 to 200	"	1	"	= 25 grains.
Cor. sublimate, 1 to 100,000	"	1	"	= $\frac{1}{20}$ grain.

Forty grains of quinine is not a very formidable amount to be given in the course of a day, or, for that matter, in a few hours, if occasion required, but the relative quantities of these other drugs seem very large; $2\frac{1}{2}$ quarts of whisky, brandy, gin, or rum; $666\frac{2}{3}$ grains of camphor, 500 grains of carbolic acid, 100 minims of oil of peppermint, 80 grains of blue vitriol, 2,000 grains of salol, 1,000 grains of tannin, 2 grains of mercuric chloride,

Calomel having little if any effect upon the germ, and opium being necessary to control peristalsis in the guinea-pig, before he can be made to take the disease, the logic of the situation seems to point plainly to quinine as the least harmful, and therefore the most efficient remedy, even in choleraic diarrhœa, or in moderately severe attacks of cholera, where the treatment may be carried through several days. How would it be in "foudroyant," "fulminant," or "explosive" cases, where if anything is to be done it must be done quickly, and enough of the remedy given in the course of two or three hours to arrest multiplication of the germ throughout the whole intestinal tract? In full view of the modern theory that such cases may be the result of toxic absorption rather than the presence of the spirilla in overwhelming numbers in the intestines, it seems but reasonable that by inhibiting the growth of the germ one may at least limit the further production of the toxines. Whatever other treatment may be used, in foudroyant arsenicism we would hardly be justified in withholding the proper antidotes for arsenical poisoning. Even in septicæmia quinine as yet holds the field against all comers.

The latest estimate from Hamburg (September 8, 1892), places

the death-rate at forty-four per cent., and the probability is that when the full count is in, the loss will closely approximate the old one of about fifty per cent. So far as heard from, the good results to above date seems attributable to hypodermoclysis. The word comes from Paris that Beta naphthol (hydro-naphthol) has failed.[1] Salol has failed, and the reason of its failure is apparent when we know that Lowenthal's 20 grammes (300 grains) daily, which according to his theory should set free in the duodenum the large amount of 120 grains of carbolic acid, only equals, after all, so far as inhibitory effect is obtained, 6 grains, or, estimating the carbolic acid alone, less than 10 grains of quinine, the 45 grains of Gonzales, of Salvador, about 1 grain, and the 120 grains daily of Nicholson, of Patna, India, less than 3 grains of quinine. Tannin entroclysis has failed in spite of Dr. Shakespeare's expressed opinion that "with such an instrument not only the whole length of the colon can be filled with the desired fluid, but also not infrequently a quantity can be made to pass the ileo-cæcal valve into the small intestine." That is to say, a small amount of the remedy be placed just where it is most needed. Quinine failed by the hypodermic method of administration in 1873 and 1884. The germ being inside the intestine, and not in the circulation, and the affinity of the remedy for the kidneys, and not for the bowel, this method of using it would seem as irrational as the administration of sulphites or sulphur by the mouth in the treatment of sycosis, chloasma, or scabies. That by this method of using quinine the damaged kidneys might be impeded in their function, and if there be aught in the old uræmic theory of blood-poisoning in cholera, this undesired event, insured by the further retention of urea and uric acid to the extent of about forty per cent. where complete suppression of urine has not occurred, is easy to understand.

To reach the seat of the disease the remedy must be given by the mouth, and the only noteworthy objection to this use of quinine is the old idea that quinine, under certain conditions, is very irritating to the stomach. In the disturbed stomach of remittant fever we do not always regard this symptom, and it was my own experience in 1873 that this remedy seemed a very good anti-emetic in cholera. In the whole history of that epidemic (Woodworth, McClellan, *et al.*) there is, if I mistake not, but once mention of its having been vomited, and

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[1] If the above rumor were not correct we should know it by this time, as it was certainly most extensively tried in Paris last year.

in that case it was given in conjunction with capsicum, not repeated, the patient put upon other treatment and dying thereafter.

Has quinine by the mouth given good results in cholera? I think it has.

Botkin, in 1871, in the *Wiener Med. Presse*, reports a loss of but 17.3 per cent. under the use of quinine. He gave 5-grain doses three or four (sic) times daily, and when vomited resorted to hypodermic injections of 8 grains frequently during the day. If the latter dose, dissolved as it was, had been given by the mouth, and in case of vomiting thereafter had been repeated until about 30 grains had been retained, and continued in smaller doses so long as symptoms seemed to require it, there might have been a better result even than the above very favorable showing.

Owing to a persistent denial on the part of the authorities at New Orleans that cholera had been imported there in 1873, the profession in the Mississippi Valley (to which this invasion was limited) was left to make its own diagnosis as to the nature of the disease then prevailing. As late as September of that year, or seven months after the epidemic broke out in that city, the New Orleans *Medical and Surgical Journal* discredited the importation of the disease, and the editor admits having considered it at first catarrhal in character. Of the eighty cases first reported, forty-six went on record as cholera morbus, "cholera Asiatica appearing infrequently." The idea of a cholera Mississippiensis was very prevalent during the early history of the epidemic in the lower valley, and throughout its entire history many physicians held to the belief of its malarial origin. This is especially noticeable in Tennessee and Kentucky. Quinine is frequently mentioned in treatment, but too often it is the last remedy of the list, and in but few cases, comparatively, is the size of the dose, the method employed, or the frequency of its administration noted. Good results occasionally obtain after 5 grain doses by the mouth, and several recoveries after rectal injections of the drug in varying quantities. One writer states that the disease was very fatal unless the patient was seen early and large doses of quinine given, and two instances are recorded where the patient recovered after the large amounts of half an ounce in the one case and two-thirds ounce in the other, had been taken. On such data, however, it is impossible to arrive at any satisfactory conclusion other than that, generally, the results seem favorable.

There is one exception to this rule, and the treatment and its

results are so very remarkable as to be nearly unique in the history of medicine, and on so large a scale as almost to force conviction. As recorded in the volume entitled "The cholera Epidemic of 1873 in the United States," the facts are as follows:

About May 1, 1873, the authorities in control of the Tennessee penitentiary at Nashville, Tenn., received notice that a malignant disease had broken out among two camps of convicts at work along the line of the Memphis & Paducah Railroad. As to how fatal it was there are several conflicting statements. Fortunately we have, on page 137 of the above-mentioned volume, the report of the chief engineer of the road, Mr. J. L. Meigs, which gives the whole number sick of the disease from May 1st to 13th as forty, and the number of deaths twenty-four, a fatality of sixty per cent. On the 12th of that month convicts to the number of seventy-five were sent back to the penitentiary at Nashville, purging and vomiting. On arrival about one-half only of this number could be accommodated at the hospital, the remainder being shut up in cells, usually two in a cell having a capacity of two hundred and fifty cubic feet of air, ventilation being through a grating, fourteen inches square, in the cell door, with the bucket that received the choleraic discharges inside the cell.

The diagnosis "scorbuto-malaria" was made by the physician of the penitentiary, and the sick put upon a diet of fresh vegetables and saurkraut, with "*tincture of iron and quinine freely given*, chlorate of potash being used as an adjuvant." The day after the arrival one man died, this man on reaching the penitentiary "being in so much better condition than the others" that he was not admitted to the hospital, but sent to his cell. A letter recently received from Dr. George P. Henry, the physician, states that this patient had no medical treatment whatever. "The remainder recovered rapidly, and in a few weeks most of them were at work." In the above-mentioned letter Dr. Henry further states that to these seventy-four cases "I gave quinine by the mouth altogether," "freely and at short intervals at first," and that "the cases were usually under control in an hour or two after the administration of perhaps 20 or 30 grains of quinine," "that finding its potency for good I kept it up," using it later on "both by the mouth and hypodermically." Dr. W. M. Wright, at that time Superintendent of the penitentiary, in a letter recently received, states: "I think that 20 grains of quinine were given in about four hours."

From May 12th to June 8th there was an average of fifty-seven

cases daily under treatment in hospital and in cells. At this last date there was an "explosion" of the disease in the city of Nashville (brought there by these same convicts), and "the fact was recognized that cholera was epidemic within the penitentiary walls." The dietary was changed in conformity to the corrected diagnosis, and during that day and the night following there were three deaths of prisoners from the disease.

On June 9, 1873, Dr. Thomas Menees, a prominent practitioner and teacher of medicine in the city of Nashville, was called in counsel, and the treatment thereafter was as follows: Calomel and opium in small doses frequently repeated, "quinine freely given either by the mouth or hypodermically." In a meeting of the physicians of Nashville, held December 16, 1874 (1873?), Dr. Henry further states, "after June 8th we treated the patients with quinine, calomel, and opium." "I called it malaria." Dr. Menees, at the same meeting, said, "we also used quinine freely," and he places the whole number treated at between four and five hundred, "prisoners and attaches." In the letter from Dr. Henry above referred to, he places the number severe enough to be called cholera at three hundred and fifty, the rest choleraic diarrhœa. Dr. Menees states that "from the 9th day of June to the 12th day of July there were twelve deaths. There were some that had chronic diseases, and when they were attacked they would die." It will be seen by the above that there were fifteen deaths after the idea that the disease was malaria was given up and the proper diagnosis of cholera made, but only one death prior to this. There are three of these cases in which it is very doubtful that they had any quinine, or if so, whether it was given in sufficient doses in the light of modern discoveries to inhibit the growth of the germ. Dr. Henry writes he cannot remember whether the three dying on June 8 had quinine or not. It will be recalled that on that date the diagnosis of cholera was made. Counting these, however, and allowing nothing for those already enfeebled by "chronic diseases," and taking the lowest figure (350) as the number of cholera patients, and the result is a death-rate of less than $4\frac{1}{3}$ per cent. *Under similar circumstances, only that the hospital accommodations were sufficient for all, the dietary arranged with reference to cholera and not to scurvy, and only a few of the diarrhœa cases given quinine in tonic doses, the death-rate in the Ohio penitentiary in this city was over seventy-five per cent.*

That the disease was Asiatic cholera, which obtained access to the

Mississippi Valley through the ricketty states rights' quarantine at New Orleans, is no longer a debatable question. The death-rate of fifty-two per cent. for the epidemic would alone show this. That it was of no mild type in the Tennessee penitentiary is attested by the fact that there was sixty per cent. of loss before the sick were ordered in, and furthermore, that there were one thousand deaths in the city of Nashville during the epidemic — a mortality of about one in thirty of the population of the city at that time. That other remedies than quinine were used is true. Tincture of iron, chlorate of potash, "calomel, and opium in small doses," camphor, "calomel inserted dry under the skin," blisters, and quinine hypodermically; but all these had been tried elsewhere and found wanting. Reasoning by exclusion the treatment other than quinine is certainly insufficient to account for the results.

To control so fatal a malady the amounts of quinine above indicated seem small, but are quite enough in view of modern developments to effect the wonderful results if continued for several days in sufficient doses to maintain the effect once gained. In my own cases fifteen grains given in the course of two hours always checked the symptoms, and three to five grains given at about two hours' intervals thereafter were usually sufficient to keep the symptoms under control. For how long a period this treatment was persisted in I cannot now recall, doubtless in most of the cases for several days, as there were but two instances [1] in my own practice in which the disease tended to return. In another case in which I was consulted the patient got fourteen grains during a forenoon, with the result of checking the disease for a period of forty-eight hours. At the end of that time the symptoms returned, the patient dying in a few hours without quinine. According to the Marseilles experimenters the germ was rarely found in the discharges after four days, and never after ten days' time. The growth of the germ in the last-named case was certainly not inhibited for a sufficient length of time, and in my own cases I suspect that it was a resultant non-specific enteritis that I had to deal with.

Fifteen grains of quinine are sufficient to inhibit growth of germ in about five quarts of fluid, in case test-tube experiments hold good

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[1] In the article in MEDICAL RECORD for October 1st, but one recurrent case is mentioned. Since then, having had access to a partial report of cases made soon after the epidemic in Cincinnati Clinic, November, 1873, the other case is recalled to memory.

on so large a scale. With the rapid peristalsis of cholera, and the very small quantity of the remedy that would be lost through absorption, the currents being into and through the bowel, it is quite reasonable to suppose that even in the intestinal tube these experiments would hold good, and the quinine, instead of being absorbed, as it usually is, by the stomach, pass onward into the intestine where it is needed. As to coincident treatment I shall not venture to make suggestions. The symptoms calling for hypodermoclysis, for small hypodermic injections of morphine, for small doses of calomel, for doses large or small of bismuth or other astringents, or alternatives in the treatment of the ensuing enteritis, are sufficiently obvious.

The statement is made above that the results in the Tennessee penitentiary are nearly unique. They would have been quite so had it not been for the Naples treatment by camphor. According to Dr. Rubini there was no death among 592 patients treated with an alcoholic solution of camphor in such manner that the patient received in mild cases about thirteen grains, and in severe sixty-six grains of the drug in the course of one hour. The latter is a convulsant dose equivalent to four grains of quinine. Tested afterward in the Whitechapel Workhouse, England, there were nine deaths out of fifteen cases of the disease. A homeopathic physician who would give such large doses could not be depended upon for accuracy of statement as to results.

[From the Medical Record, April 29, 1893.]

The Remote History of Quinine in Cholera, with Summary.

THIRD PAPER.

(In the very commencement of this paper I wish to return thanks to Major J. S. Billings, Surgeon, U.S.A., and Librarian, S.G.O., Washington, D.C., for calling my attention to these earlier authorities and putting the same at my service. In my second paper I had carried the meagre later history of quinine in cholera back through the journals at my command to Botkin only, in 1871, and the hypodermic use generally. My thanks are also due to Major A. A. De Loffre, Surgeon, U.S.A., for rendering into the vernacular a number of French authorities; to Dr. A. M. Bleile, Professor of Physiology, Ohio State

University, for translations of the invaluable German and Dutch writers; to Dr. Henry Liddell, Washington, D.C., for translations of Spanish, Italian, Portuguese, and Russian authorities.)

In an article entitled "A New Specific Method of Cure in Epidemic Cholera, or, more properly, Cholera-Fever, by the Antifebrile Principle of Cinchona Bark," Hanover, 1831, occurs the first mention that I have found of the use of this agent in cholera. The writer cites two physicians in India, who, in 1762, recommended "on the least remission in the cholera-fever to give bark." The anonymous author of the pamphlet suggests "that opium be regarded only as an adjuvant, the cure to be expected from quinine." His argument is theoretical entirely, based upon the supposed malarial character of the disease and his own experience in isolated cases of what appear to be bilious diarrhœa and cholera morbus, the author never having seen a case of Asiatic cholera.

Mr. C. Negri, London *Lancet*, February 1, 1832, commenting on an earlier case of Mr. S. R. Ensor's, says: "I am strongly inclined to believe that had Mr. Ensor substituted bark for opium and brandy, his success might have been more fortunate, and I am the more inclined to this belief because it has been but a short time ago since I had an opportunity of seeing two very similar instances which presented more severe symptoms and were perfectly cured by the free administration of bark alone." Then follow two cases that appear to be tertian or quartan malarial diarrhœas, successfully treated by bark. It must not be forgotten, in this connection, that cholera was prevailing in England at the time, and that true choleraic diarrhœa often assumes an intermittent form.

Mr. S. R. Ensor, London *Lancet*, March 3, 1832, after referring to the same fatal case, adds: "Within the last month I have seen three similar cases of a milder character, and have found the preparations of cinchona highly advantageous when a determination to the skin had previously been established. But when the surface of the body has become cold, corrugated, and dry, the bark has invariably proved emetic."

Dr. Bluff, Aix la Chapelle (*Journal Chir. und Augenheilkunde*, April, 1833), precedes his cases by a long discussion to show the relation of intermittent fever to cholera. He gives a report of seventeen cases treated by himself with quinine; two grains every fifteen minutes at first, and every half-hour after symptoms were under control for a

varying period in cases that recovered, resulting in thirteen recoveries and four deaths.

He further remarks, "of these thirteen, six were the most virulent cases of cholera that could well be imagined. Of the four that died, one had had choleraic diarrhœa for four days before taking any medicine, and was in *statio mortis* when I was called. Another received the medicine regularly, but after every tablespoonful of the quinine mixture received a glass of brandy (four an hour) to take away the bitter taste," etc. (The first record of the ill effects of alcoholics in this review.) "The other two cases were amid the worst possible surroundings, and only one who died was a robust young person." He further recites: "Dr. Stephen, of this city, also treated eight cholera cases successfully, giving (after an emetic) a tablespoonful every half-hour of a solution of eight to twelve grains sulphate of quinine; twelve to sixteen grains alum in four ounces mint water. After several hours (at most six) reaction set in and patients recovered." Twenty-five cases, all told, with four deaths — mortality, sixteen per cent. There occurred altogether in Aix la Chapelle 427 cases; 205 recovered and 222 died. Evidently malignant cholera Asiatica, with a mortality of 51.9 per cent.

Dr. Kosser, Posen, same journal and date, after remarking on the analogy between cholera and pernicious intermittent fever, its effects upon the solar plexus of nerves, and recommending litigation of the four extremities ("which will retain sixteen to twenty ounces of blood"), goes on to say, "As all medicines which have been hitherto used in cholera have done no good, I thought of the use of large doses of sulphate of quinine. . . . I used six grains of quinine with a half-grain of extract hyoscyamus every two hours in the first case." "After seeing the good effects in the first patient, who was sick to the highest degree, . . . I became bolder, and gave it in the most dangerous cases every fifteen minutes, nay, every ten minutes, in the same doses. . . . With this treatment of eleven cholera cases, all affected in the highest degree, I cured ten. The eleventh, who had improved after the use of this remedy, but whom I had to leave for eight hours, I found on my return in complete paralysis, and died in forty-seven hours after beginning of disease. . . . In addition to these sick soldiers I treated five civilians in the same way, all recovering. Later, cholera invaded the Eighteenth Regiment. I saw the sick. . . . They were treated according to the experience laid down in literature. They all died, however. . . . After a few days I was called to the

civilians' hospital. I found a patient in the highest degree of paralysis; he was forty years old. For fourteen hours he had had continuous vomiting, and forty diarrhœa discharges. I gave him sulphate of quinine. On my return, after one hour, the vomiting had ceased, and he felt somewhat easier. He now received the second powder, and three hours later the third. Symptoms all improved, but diarrhœa not entirely controlled. I left three powders, to be given at two hours' interval. On my visit in the morning I found the bed empty. I was somewhat startled, but soon the patient came out of the kitchen smoking a pipe. Convalescence went on uninterruptedly. This case was followed by four other soldiers. They had immediately the most violent symptoms—hoarseness, vomiting, diarrhœa, ice-cold and blue extremities, intense cramps in the stomach and calves, the pulse not to be felt. These patients received every half-hour six grains quinine with one-half grain extract hyoscyamus; ligates extremities, etc. Vomiting and cramps ceased after second or third powder. Later I gave these powders in some severe cases every ten minutes, and sometimes gave two at once—powders given with coffee or wine. In a few cases violent symptoms returned in twelve to twenty-four hours (intermitting from incomplete inhibition?), and after second to fifth day all symptoms of cholera had disappeared. During the next fourteen days I treated seven more men from the Eighteenth Regiment. They all recovered except one man." To another case of foudroyant cholera in a soldier on guard duty, he gave an emetic followed by quinine in heavy doses, with recovery. Thirty cases with two deaths —a mortality of 6.6 per cent. only. The reckless use of hyoscyamus here would seem to disprove Hamlet's suspicions in regard to his father's "untimely taking-off" by reason of the "accursed hebbene" stuffed into his ear by his worthy uncle. In neither case could it have been absorbed.

Dr. Antonio Putelli, Venice, *Annali Universali Medicina*, Milan, 1836, "On the Use of Sulphate of Quinine in High Doses in the Cure of Cholera Morbus Asiatica administered in the Algid Stage." This author considers that cholera morbus Asiatica affects the nervous system of the "vita organica." He cites no particular case or cases. While he boasts that "he has seen his patients in a short time cured and quickly brought to convalescence," he "is compelled to admit that in the case of cholera fulminante the therapeutic described has but little effect." In the algid stage of cholera, accompanied by vomiting, and also up to six or eight hours after the disease has developed,

I prescribe forty or fifty grains of sulphate of quinine, mixed with two or three grains of opium, and the whole made into five or six pills (eight grains each), to be taken every hour, diminishing the dose according to the condition, sex, individual, constitution, etc. If the first pill be rejected I give another, and a third, fourth, etc., if necessary, until retained. I have never seen more than three pills rejected, and the disease is soon tranquilized and the alvine dejections thickened." He gave the remedy to children in a mixture containing alcohol, and also used clysters of a decoction of calisaya. "On the second day I gave fifteen or twenty grains of the sulphate. . . . Such was the therapy adopted by me in many cases, amounting in four years to sixty persons of both sexes, of whom thirty-two were cured." A report very vague and unsatisfactory, but given for what it is worth. That Dr. Putelli should felicitate himself so highly upon the recovery of about fifty-three per cent. only of his cases would seem to indicate that the epidemic in Venice was exceptionally malignant. That he would have had better results if the quinine had been given in powder or in solution I do not for a moment doubt. It has not been my custom to prescribe quinine in pill form for persons suffering from serous diarrhœas since a patient in the early years of my practice commended very highly the efficacy of some quinine dragees that I had given her, because the next passage from the bowels after taking one she always heard the pill shoot into the vessel. On inspection I found her report correct. An eight-grain pill, made up with one of the old excipients, acacia or tragacanth, would, with the rapid peristalsis of cholera, ricochet down the intestinal canal, tearing through a spirillum bower here and there, and after doing some mechanical violence to that delicate exotic, be found in the stools soon after, if search were made.

Dr. Thomas Close, Portchester, in *The Scalpel*, New York, July 25, 1849, reports one case of cholera getting well promptly on one dose of twelve grains by mouth, with a like amount, together with a teaspoonful of laudanum, given by rectal injection two hours thereafter. Many cases of dysentery and some of the severest attacks of diarrhœa (prevailing at the same time) yielded at once to twelve-grain doses of quinine.

The same number of *The Scalpel* quotes from two lectures given by Dr. C. W. Bell, on cholera and intermittent fever, Manchester, England. After discussing his very elaborate theory of the disease, he says: "If I have overrated the effect of the medicine recommended

(sulphates of quinine and iron) I have not been induced to do so by theory alone, but after I had used it in many thousand cases. . . . While the epidemic prevailed in Teheran, my court-yard was daily crowded with hundreds of poor wretches praying for the love of God for a supply of the bitter water. It was served out to them in pint-and-a-half mixtures, containing twelve grains quinine, nine of sulphate of iron, and thirty drops of dilute sulphuric acid, with directions to take a coffee-cupful at a dose. . . . In some of the most remarkably rapid cures the whole was swallowed at a draught." Only short extracts from lectures are given. The title of the article in the index of *The Scalpel* reads, " Dr. Bell's Lectures on Cholera, Five Thousand Cases Cured by Quinine in India." This smacks somewhat of Marco Polo, but like the famous traveler he had doubtless seen something of that which he wrote about.

Dr. B. F. Sargent: *Philadelphia Medical Examiner*, September, 1854, in " Notes of a Few Cases of Cholera Treated in the Summer of 1849, showing the Comparative Curative Powers of Sulphate of Quinine in Large Doses," mentions that the " late Dr. Wilson " attended these cases in conjunction with himself.

This article deals only with " treatment we pursued in the collapse of cholera. . . . We say nothing of the simple diarrhœa which recovered under ordinary treatment. He refers to article in London *Medical Gazette*, 1847–48, in which Dr. C. W. Bell's treatment is mentioned, as giving the clue to the use of quinine in these cases. Following this come cases treated by calomel, opium, acet, lead, quinine in small doses, chloroform, etc. He mentions the use of large doses of the remedy in pernicious intermittent fever. Then follows a narrative of cases treated by quinine, *typical, unmistakable Asiatic cholera of gravest form.* The dose given at commencement of treatment varies from ten to twenty grains in the course of an hour or two, either in one or two doses, usually with laudanum and brandy, and followed by smaller doses of quinine for a varying period thereafter. " To recapitulate, we have cited in all thirty-seven cases of cholera in the stage of collapse. Of these, seven were treated with calomel and opium, sugar of lead, etc., and of this number only one recovered. Four cases treated by Dr. Ayers's plan (calomel, 1 gr.; laudanum, 1 gtt.; every five minutes), all died; four by chloroform, camphor, or oil of turpentine, all died; three by quinine and sulphate of iron in small doses, all died; seventeen by quinine in large doses, with thirteen recoveries and four deaths; two by bleeding, both recovering. In these cases the

prompt cessation of vomiting and diarrhœa and the prompt reaction are especially noticeable. Of the four fatal cases treated by quinine in large dozes, one, a nurse, had been sick a week with premonitory diarrhœa—she partially reacted; another, having vomited two fifteen-grain doses of quinine, was treated with rectal injections of quinine thereafter; the third case was drunk for three days previous to the attack, when treatment commenced was thoroughly collapsed and nearly pulseless—two twenty-grain doses of quinine given; fourth case not narrated. Fatality, 23.5 per cent."

Dr. W. Strange,[1] after stating his theory of the disease to be essentially that of Dr. Bell, having treated by other means thirty-one cases with nine deaths—a fatality of twenty-nine per cent; had nineteen cases that he afterward treated with quinine, with four deaths—fatality twenty-one per cent.

Gave only two-grain doses of quinine, with twenty drops of tinct. ferri chlor., every two or three hours; recoveries slow, the doses of quinine being too small. He notes immediate effect of quinine in checking the vomiting. Two cases that died under the treatment were intemperate. He notes that "the choleraic diarrhœa was curable by one or two doses of the quinine and iron, while they obstinately resisted treatment by stimulants, opium or calomel."

Here comes trouble! In the leading article, *Medical Times and Gazette*, London, October 8, 1853, occurs this: "But of all remedies used during previous epidemics, with the exception, perhaps, of opium as a palliative, . . . quinine, probably, is most deserving of a further trial. Modern experience in India is leading to increasing confidence in its powers. Toward the close of the epidemic it was used in London. *Mr. Spencer Wells injected a solution into the veins in four cases. Dr. E. A Parkes did so in two others; all died.*"

As they most properly should, that method of administration being as useless in cholera as the hypodermic. In the same journal are reports of cases treated by Drs. Wells and Parkes.

Dr. J. Sappington,[2] on "Quinine in Cholera," with much selective polytherapy, gave quinine in one grain doses for consecutive fever, only—none in the cholera stage—with asserted good results. Had he given it earlier and in larger doses, there might have been no consecutive fever.

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[1] Letter to Dr. C. W. Bell, Provincial Medical and Surgical Journal, London, 1849.

[2] Eclectic Medical Journal, Cincinnati, 1849.

Dr. Thomas W. Gordon, Georgetown, O., in *Ohio Medical and Surgical Journal*, 1853, gives a report of eighteen cases occurring in Georgetown and vicinity in the summer of 1852. *Undoubtedly cholera, most of the cases described being typical and severe in form.* Twelve cases treated by himself and brother, by quinine and morphine, in the doses of the former of from two to ten grains, at intervals of ten minutes to six hours (*pro re nata*), recovered; of the six cases treated by others and otherwise, five died. He notes the absence of consecutive fever, but speaks of one of the fatal cases becoming intermittent before death. Elsewhere[1] he states, "I do not expect that quinine will cure every case, but believe it just as certain to cure cholera when properly administered as it is of curing regular intermittent fever." Quinine given in powders.

C. Vianna, *Gaz. Med. de Lisbon*, February, 1856, describes a case of what appears to be malignant cholera supervening upon an intermitting febrile attack, and with a consecutive fever of similar character, recovering on quinine, eight grains in two hours, followed for several days by varying quantities of the same drug at varying intervals. Treatment at the cholera hospital, with sulphuric acid lemonade for vehicle. I insert this case more as a protest against the custom of asserting cases cured by quinine to be necessarily ague, than for any other reason.

Don Clemento Ascarza, in *El Siglo Medico*, Madrid, 1856: "Happy Results Obtained with Sulphate of Quinine Given in Large Doses in the Algid Stage of Cholera." He notices an apparent intermission in symptoms otherwise those of a grave form of cholera Asiatica. That he was on the lookout for such remissions, and that we must eliminate this "personal equation," as is done in astronomical calculations, is evidenced by his citing Torti. He gave forty-eight grains quinine in four doses, in pill form, at hourly intervals; improvement, but final outcome of first case not stated. Five other cases that had received "extreme unction" recovered under the treatment. That there were one hundred and forty-seven cases in the city and only five that passed into the algid stage would indicate either a mild epidemic of cholera or one equally mild of gastro-enteric malaria.

Dr. Vial, in a letter to the editor of *L'Union Medicale*, September, 1860, states that he used the medicine with happy results. Dose and method not given.

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[1] Transactions of Ohio State Medical Society, June, 1855.

Here come sweetness and light, however, and they come from the Dutch country, that Campbell has recently shown to be the source in our own land of much of what we have been accustomed to thinking our Anglo-Saxon institutions, among which may be mentioned the equality of man; the separation of Church and State; the town meeting; the free school, and the relation of separate states to a national government. The writer's name is Dr. J. L. Pompe van Meerdervoort, "On the Treatment of Cholera Asiatica by Quinine Sulphate in Japan, *Nederl. Tijdschr. Geneesk.*, Amst., 1865. He says:

"During my residence in Japan, from September, 1857, to November, 1862, I passed through three different fearful epidemics of cholera. In these three epidemics I personally treated 2,467 patients, all without a doubt affected with cholera; of this number 1,746 recovered and 721 died. This result is very favorable, about seventy per cent. saved, and about thirty per cent. dying, especially when one considers that in many cases I was not called at the beginning, or soon after, and that I was the only physician in a city of 60,000 inhabitants (Nagasaki), which, so to speak, would prevent a proper control of the epidemic. This favorable result I ascribe to the treatment with the sulphate of quinine." The epidemic was brought to Nagasaki by the American ships Powhattan and Mississippi from China. It came in the time of the fruit harvest, and the Japanese, according to the doctor, "eat no ripe fruits and sleep half-naked on their verandas." His first and second reasons for using quinine were the prevalence before the epidemic of malarial troubles. "3d. Several of my colleagues in Netherlands, India had previously used quinine in cholera with great advantage. 4th. All other recommended medical treatments had been of no avail." After recommending its use as early as possible, he goes on to say: "If vomiting is severe and continuous the remedy will not be tolerated any more, and one had better then resort to hypodermic injections, which were then, as yet, unknown to me." Very fortunately so, as had this method been resorted to, the favorable results in so large a number of cases, and under the circumstances above indicated, would not have been obtained. He recommends in the commencement three to six grains of quinine dissolved in sulphuric ether, alcohol, and peppermint oil. "Should symptoms become worse, however, and vomiting, cramps, and abdominal pains come on with the well-known cholera excreta, then one should give, every half-hour, four to six grains of quinine, with warm bath." He uses champagne and ice for vomiting, and says, "I very seldom use narcotics, especially

in large does. . . . Often, nay, almost always, did I see distinct collapse come on in those sick to whom the Chinese doctors gave large doses of narcotics. . . . Bleeding, which was used in the beginning of the epidemic of 1858 by the Japanese physicians, usually caused death. As soon as the crisis has appeared one should continue for some time the use of the quinine, as otherwise there is danger of exacerbations, during which the sick may yet die. Later, the dose may be decreased. . . . There need be no fear of quinine intoxication. . . . I saw this intoxication but three times, and warm baths, cold affusions to head, port wine and beef-tea soon obviated these symptoms." The writer shows his theory-bias by the remark: "The use of quinine in cholera or similar malarial epidemics is to be recommended, especially in the tropics. . . . I do not wish to say that I consider it as a certainty that pernicious fever and cholera are identical."

"The cholera mixture I prescribed in Nagasaki has the following formula:

℞	Sulphate of quinine	1 drachm
	Dilute muriatic acid	1 drachm.
	Alcoholic sulphuric ether	1½ drachm.
	Eleo-sacch. menth. pip	2 drachms.
	Pure water	8 ounces.

In mild cases one tablespoonful every half-hour; on improvement, every hour; in severe cases one tablespoonful every quarter hour; on improvement every half-hour, and then in decreasing doses. After a short use of the above mixture there is usually improvement, at least if it is used in time. . . . The number—2,467—here given, pertains only to those cases treated by me personally—*all severe and well developed cases of cholera—not cholerine.* Of these one-sixteenth were treated in hospital, fifteen-sixteenths outside in the city. The Japanese physicians who followed my treatment obtained just as favorable results."

The hypothesis is often used as a method of arriving at accurate results in the exact sciences Let us suppose that instead of one physician to 60,000 people, there had been the usual ratio obtaining in the United States, of one to five hundred population; that instead of a vegetable and fruit-eating population (the Buddhist priests in Japan have only in the last few years begun to frequent the butcher stalls) there had been a better fed people of a stronger vitality to deal with; that instead of seeing these cases only in the severest stage of cholera,

they had been seen during the earlier stages of choleraic diarrhœa, or so-called cholerine, what an enormous reduction in the mortality might have been secured by this treatment can best be judged by the results in the Tennessee Penitentiary in 1873, of which more anon. The more exact mortality of Dr. Van Meerdervoort's cases was 29.22 per cent. W. O. Shakespeare says, "In Japan in 1854, there occurred 154,373 cases, with 101,695 deaths, a mortality of 65.8, showing the ordinary severity of the disease in Japan."

Dr. A. Schlomann[1] says: "In the cholera epidemic of the Mississippi Valley and the Gulf States, summer and fall of 1866, several American physicians obtained surprisingly good results from the sulphate of quinine. Such a coincidence might seem strange, but is explained, however, by the fact that everywhere in these States the appearence of cholera came during the time for intermittent fevers. This would tend to experimentation with quinine salts, which are the staple drugs of the Southern pharmacist. . . . *Our cholera was the real cholera of the Ganges Delta and not a doubtful hybrid form of intermittent.* . . . The following observations were made during the epidemic in San Antonio de Bexar, a town in Western Texas, having a population of 10,000 souls. . . . The outbreak of the epidemic was preceded by the usual endemic and intermittent fever, which, however, was not of a malignant type, and was declining before the cholera came. . . . In these cases (non-febrile choleraic diarrhœas) I carried over the quinine treatment with the same unvarying good results. The constancy of success and the continued immunity of my *clientèle* in the midst of the prevailing great mortality, caused me to wonder whether this result was due to the medicine or to other accidental and unknown conditions. To find this out, I concluded to change the quinine treatment for opium, and aromatic and astringent remedies. . . . During the first half of the new day everything passed off pleasantly, and the diarrhœa seemed to be checked in all cases. During the night, however, after the effect of the opium (quinine?) had passed off, diarrhœa returned in every case, and worse than before. The discharges became so threatening that I speedily returned to the use of quinine. After this day I continued the quinine treatment with the same previous good results, so that at the end of the epidemic I had come to the conviction that quinine

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[1] Treatment of Asiatic Cholera by Quinine, Ber. klin. Wochenschr., September 4, 1871.

would be, at some future day, of the same importance in the treatment of cholera as it is in the treatment of intermittent fever." (This writer had formed the theoretical opinion that quinine would do only harm in the "asphyctic" stage, and so did not give it in his worst collapsed cases.) "I wish to remark that all cases that came into treatment in the asphyctic state and all lighter ambulant cases of diarrhœa have been excluded. Under the quinine treatment 220 cholera and cholerine [2] patients recovered and three died. Mortality, 1.3 per cent." Then follows a history of these three fatal cases.

"1st. Vomited the medicine, becoming an hour thereafter 'cyanotic' and died.

"2d. Intestinal diphtheritic form with complete anuria; thirty grains quinine did not arrest disease. He died on fifth day.

"3d. A child, three or four years old, that got only five grains of quinine died."

Commenting on these three fatal cases, he goes on to say: "In regard to these three cases, which might be used as testifying against the value of the medication, the first needs no further comment. In the second the medicine was absolutely without effect. The tenesmus present makes it probable that the disease was located in the large intestine, and I regret, with my present views, that I did not give a quinine clyster. The method of treatment was always the same, with small modifications. I always carried gramme doses of quinine, and a morphine solution for the purpose of hypodermic injection. The quinine was always given without delay, either in half or whole dose, and repeated after the next evacuation, or also after two or three hours if there was not a slight intoxication. Generally opium was added to this. In vomiting or nausea often a subcutaneous injection of morphine was given." Bases his objection to use of drug in the asphyctic state on the fact that he had seen "disastrous results" from using it in the "fever period of remittent or in typhoid fever," a doctrine hardly of universal acceptance even at that time, and certainly not now. He quotes other authorities, and mentions hypodermic use of the drug.

The French authorities are of but little moment. In 1865 M. Pidoux recommended it in tonic doses — a "weak mixture," containing one-third grain of quinine to the dose; a strong mixture containing

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[2] German nomenclature—choleraic diarrhœa, cholerine, cholera; French—cholerine and cholera only.

about one-half grain to the dose. Following his treatment, Dr. O. Des Broulais used it in what appears almost certainly to have been an epidemic, malarial in character, but attended by intestinal disorders, in the Valley of the Loire Inferieure, with asserted good effects. Mention is made that these small doses seemed to have had a beneficial effect upon the vomiting.

In *L' Abeille Medicale*, 1865, Drs. Bourgogne and B. de la Grandiere dispute over a case of cholera (as asserted by the former but denied by the latter) that was cured by tannate of quinine *after reaction had taken place.*

L. V. J. Gruzof, Process Imperial Medical Society of the Caucasus, 1871, states that "in the summer of 1866, in Abchasia Huduat, the author had charge of the cholera division of the regiment." He gives no figures, but says the death rate was small under the quinine treatment. Further on he gives two mild cases of cholera (cholerine?), occurring in 1871, successfully treated by hypodermic injections of quinine. He also criticises Professor Botkin, of St. Petersburg, for using four to five grains of quinine by the mouth as "entirely inadequate and too risky;" recommends the hypodermic use instead, and finally adds, "the very small percentage of death-rate (17.3 per cent.) in the treatment of cholera with quinine in Professor Botkin's clinic and my own personal preference for the hypodermic injection method, lead me to make the present communication." It may be recollected by some that in recording Professor Botkin's results I said in my last article in the MEDICAL RECORD that had Professor Botkin given the larger doses, eight grains in solution, by the mouth, and when vomited, promptly repeated the dose instead of resorting to the hypodermic method, "he would have had still better results than the above very favorable showing."

"For truth is this to me and that to thee."

My two records meet here and contain all that is known or accessible to me pertaining to the use of quinine in cholera. When my attention was called, in the Columbus Academy of Medicine, to Stillé's summary of results on board the Belleisle, [1] in which, with varying results under other treatment, out of the number (nineteen) treated by quinine, twelve died, I stated that "I had no doubt that the hypodermic method was used." Later, in writing to the friend, in Washington, D. C., who kindly looked up the reference for me, I modified

[1] Medical Times and Gazette, 1866, vol. ii., p. 590.

this judgment by adding, "or only the worst collapsed cases were so treated." How nearly my judgment, based on my researches at that time, came to being correct will be best shown by the following extract from the article entitled "Treatment of Cholera on Board the Belleisle."

1. "Quinine treatment consisted in the hypodermic injection of twenty grains of quinine in solution. * * * * * * As this plan of treatment was new, the worst cases were selected, all but two being in a pronounced stage of collapse on, or soon after, admission." It was the hypodermic method, used in the worst cases, too.

On the British flag the sun never sets, and the British drum beats round the world. Wherever that flag floats and drum beats are British surgeons to whom come these great London journals. The cases of Messrs. Spencer Wells and E. A. Parkes, experimented upon in 1853 and dying after intravenous injections of quinine, must have had their effect, as these cases were noted everywhere. In the sixties it will be recollected that the great rage for hypodermic medication was on, and here comes another failure by this "new method of treatment," and this report, too, went its rounds, undoing much of the work that had been done by these earlier writers whom I have here recorded. Strange enough, the lack of success by this method did not excite a return in any great degree to the earlier method of administration. It is my belief that the hypodermic method was more commonly resorted to in the epidemic in the Mississippi Valley in 1873 than the other by the mouth. That it was so in the city of Nashville, Tenn., I am convinced, and for the following reasons:

1. The method is not mentioned as having been used in the penitentiary until the very able counsel came in from the city.

2. Another practitioner of equally high reputation, [1] writing me, says, "I also gave quinine freely, using an ethereal solution hypodermically."

Furthermore, the number of deaths in the city — 1,000 — show either that there were about two thousand cases in the city, giving the usual fifty per cent. rate of mortality (the rate for this epidemic of

[1] I know that these Southern gentlemen will view this statement in its right bearing, analysis, not criticism. It is my belief that there are no better physicians anywhere than in Nashville, and if I am correct in my above surmise, in using this method they were following the lead of the advanced thinkers in the profession the world over.

1873 in the Mississippi Valley being fifty-two per cent.) under other treatment, or else the death-rate in the penitentiary carried into the city would give the astonishing result of over 33,000 cases of all grades of the disease, some 5,000 more cases than there were people then resident in the beautiful capital of the brave old State of Tennessee. In this estimate I have taken the highest number of cases mentioned: "There were about five hundred prisoners and attaches at the penitentiary, and almost every man, woman, and child there were afflicted with the epidemic." The number of deaths of those having medicinal treatment being fifteen, gives the rate of three per cent.

That the penitentiary cases [2] treated by quinine were malignant cholera is evidenced by the fact that it was malignant cholera, with a death-rate of sixty per cent., before the seventy-five convicts were brought in from their camps along the railroad; that it was malignant cholera in the one of the seventy-five prisoners who received no quinine; that it was malignant cholera in the negro (McClellan, quoted by Wendt), discharged from the penitentiary and dying in the city a few days afterward; that it was malignant cholera on the day when the physician of the prison corrected his diagnosis, changed the dietary of the sick, and presumably modified his treatment, as three died on that day; that it was *more* malignant cholera after other treatment was in part even introduced, twelve cases dying thereafter; that it was *most* malignant cholera that was introduced into the city of Nashville by these same convicts.

As to the cause of the results obtained, it was not the dietary, for that was arranged for scorbuto-maleria and not for cholera; it was not the hygienic surroundings, for two prisoners, for the most part, were in one cell with 250 cubic feet of air-space, and the slop bucket to receive the discharges within the cell; it was not the other treatment, for this had given a mortality of about fifty per cent. in previous, as it has in subsequent, epidemics; it was not faith-cure, for in Western penitentiaries they do not "batter the gates of heaven with storms of prayer."

It must have been the quinine first given, "by the mouth wholly," by Dr. Henry, and continued thereafter, with rare good sense and judgment, by the consultant, Dr. Menees, who doubtless saw the

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[2] For details of epidemic in Tennessee Penitentiary, see Cholera Epidemic of 1873 in the United States, or my own article, MEDICAL RECORD, December 10, 1892.

good results inuring from its use and continued it, "*freely by the mouth, as well as hypodermically.*

SUMMARY.— After writing the above, I waited for a few days before completing this paper in order to hear from my translator in Washington, D. C., to whom I had written to please verify his translation in the Putelli article above quoted, as from the large amounts of quinine taken there should be a better result than the forty-six per cent. death-rate, even with the pill form of administration of the remedy. The following extracts from his reply speak for themselves: "I regret to find on reference to Putelli that there is an inaccuracy in the translation of the passage relating to the results obtained by the administration of quinine in cholera. The true translation is, 'Such was the cure by me adopted in many cases in persons aged from four years to sixty, and of diverse sex, of whom two thirds were cured.' Mortality thirty-three per cent."

When upon the results of treatment alone I can say of Stille's list the remedy must have been given hypodermically and not by the mouth, and for the like reason in Putelli's case suggest where the translator has erred, it would seem that we had the Asiatic scourge between the hammer and the anvil, and a step had been taken by therapeutics toward a place among the exact sciences. The report of Putelli and my remarks upon the same I shall permit to stand as they are above. The pill form used will still serve to explain why the recoveries fell so low as sixty-seven per cent.

1. In my first paper [1] are given the results of treatment of cholera by quinine, in 1873, among my own *clientele.* The cases were few, but the end attained such as to satisfy my own mind that the remedy had a remarkable effect over the disease. In my second paper [2] the inhibitory list of Koch, with additions of Lowenthal's salol and Cantani's tannin are discussed, with amounts of these remedies furnishing the inhibitory equivalents of forty grains of quinine. It is my belief that this comparison has shown that quinine is the only one of these that can be given *ad libitum ad inhibitum.* In both of these papers I pointed out the error into which the profession had fallen in giving the remedy hypodermically instead of by the mouth, the germ being inside the intestine, and the emunctory through which the drug escapes being the kidneys.

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[1] MEDICAL RECORD, October 1, 1892.
[2] Ibid., December 10, 1892.

2. As to special symptoms all authorities agree that quinine in almost all cases very shortly stops vomiting, this being remarked even by the French authorities who gave it in very minute doses. In the report of McClellan *et al.*, it is only once mentioned that the remedy was vomited.

3. That in the few cases where the quinine was persistently vomited the patient always died.

4. That the diarrhœa was usually checked within a few hours, rarely lasting on for a few days when the dose was large.

5 That where the dose was sufficient reaction promptly followed the cessation of these symptoms, that there was no consecutive fever, and that convalescence was rapid as compared with that resulting from other remedies.

6. Furthermore it appears from this record that doses at the rate of about ten grains per hour for a sufficient time, seemed usually to give as good results as larger doses, and much better, generally speaking, than smaller amounts.

7. That these results did not depend upon the sulphuric acid, the hydrochloric acid, or the various salts of iron with which the quinine was sometimes combined, as quite as brilliant effects came from the quinine powders alone, given by many.

8. That the hypodermic syringe should be used only (if at all) for the small morphine injections that may be needed to control certain symptoms — pain, spasm, etc.— as in all cases mentioned where bad results were obtained this method or the intravenous was used. If bad results ever came from administration by the mouth, there is no record of the same.

9. That the pill form should be eschewed.

10. That the above results strongly confirm the belief that Koch's germ is the true cause of cholera; that it is confined to the intestinal tract, and that quinine, inhibiting in strength of one to five thousand, is the "quinine of cholera" that Semmola wished for but could not find.

11. It is the uniform testimony that although the remedy seems sometimes to have been given in very, probably needlessly, large doses, yet no very unpleasant effects resulted.

12. That the objections that the disease was not cholera but malaria successfully treated by quinine;[1] that it was only a mild form

[1] The germ test cannot be made retroactive. What method of diagnosis was pursued in the cases from which Koch first obtained his comma bacilli?

of the disease which would get well under ordinary treatment, are alike set aside by the above chronicle.

13. That the curative effects of quinine in cholera are only less certain and sure than in malaria because of the greater rapidity with which the former poison acts. The control of the remedy being as evident in the one disease as in the other.

14. That in fulminant cases the thing to do is to fulminate the quinine more rapidly—lightning strikes up as well as down.

15. That in cases of obstinate vomiting entero-clysters of quinine, forty to sixty grains in two or three quarts of warm water, should be made trial of. There would be an inhibitory margin for four times the amount of fluid mentioned, and some of this might be got beyond the ileo-colic valve.

16. That after thorough quinine inhibition in collapsed cases hypodermoclyses may be made use of with a better hope that the saline solutions will not only temporarily galvanize the patient into life in order that he may again collapse when the intestinal discharges once more set in.

17. That there is a limit in therapeutics; "we cannot make a withered palsy cease to shake," and resurrections from the dead are few, far between, and none too well authenticated. Quinine will not cure heart-clot.

The following tables seem to show about what the rate of mortality has been heretofore (the quinine having been given by the mouth):

IN JAPAN COLLAPSED AND COLLAPSING CHOLERA.

	Number of cases.	Deaths.	Percentage of mortality.
Dr. Van Meerdervoort	2,467	721	29.22

IN EUROPE AND AMERICA, COLLAPSED AND COLLAPSING CHOLERA.

	Epidemic.	Number of cases.	Deaths.	Percentage of mortality.
Dr. Bluff	1831–36	17	4	23.5
Dr. Rosser	1831–36	30	2	6.6
Dr. Close	1849	1	0	0.0
Dr. Sergeant	1849	17	4	23.5
Dr. Strange	1849	19	4	21.0
Dr. Gordon	1852	12	0	0.0
Dr. Fullerton	1873	5	0	0.0
		101	14	About 14.0

SICK-ABED CHOLERA, COLLAPSED, COLLAPSING AND QUININE-INHIBITED CHOLERA (choleraic diarrhœa, "ambulant cases," Dr. Schlömann; "that came at sick call," Dr. Henry excluded.)

	Number of cases.	Deaths.	Percentage of mortality.
Cases in last table	101	14	14.0
Dr. Stephen (Aix-la-Chapelle), 1831	8	0	0.0
Dr. Schlömann, 1866	220	3	1.3
Dr. Henry, 1873	350	15	4.2
	679	32	4.8

This is all I have to present. Were it a gun warranted to kill two hundred thousand men in one campaign, wounding as many more, I would have no doubt as to its prompt recognition in Europe. Were an enemy's fleet to "sail yonder round by the hill," or an armed universe set foot upon our shores, how quickly would we spring to arms! how soon be heard the old war refrain, "We are coming, Father Abraham," four or five millions more! That sound as "of a trumpet on before" would penetrate the "dull, cold ear of death," and from Maine to Texas all but rouse the sleeping heroes in the "bivouacs of the dead."

Of course thus far this defence against the pestilence has been but sharp-shooting, or at the most squad or platoon firing here and there, for sixty years. But wherever this resistance has been made, effective work has been done. Let us suppose that instead of this desultory method, when again the foe is among us, we attack in force all along the line, an army of life savers, seventy thousand strong, from the Lakes to the Gulf, Union and Confederate. If, after one charge of this sort we do not gain a victory over this death, and plant the American flag on the last of the major universal epidemics, there would seem to be no use reasoning in the therapeutics of cholera either before or after the event.

But heroics are for war, not for pestilence; for slaying, not for saving alive; for gunpowder, not for quinine.